510

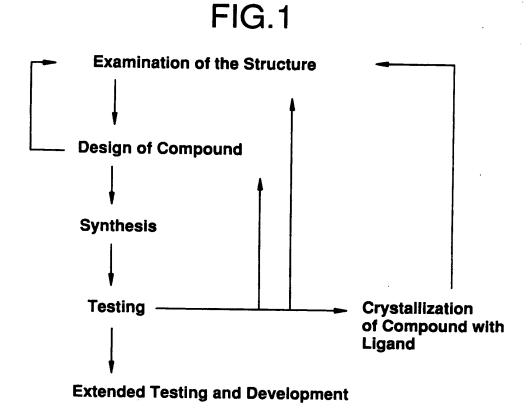


FIG.2

DOMAINS:	NH ₂ -TERMINAL	DNA BINDING	LIGAND BINDING
DOMAIITO.			

HOMOLOGY: Hypervariable > 40% About 20%

FUNCTION: Transactivation DNA Binding LIGAND Binding
Dimerization Dimerization
Transactivation
Nuclear translocation

Hsp binding

DRAFTSMAN

DRAFTSMAN

FIG.3A

•	•	•	•	•	•	155
YHDSVRDADY	SATVAESMGL YMDSVRDADY	IKTELESKEL	NNRPGILISD	Sept. Cr. Co.	NO L KOOONEN	F 3.5
200101				0511 005	Nanoccent	ל א ע
LDSVIDTI A	SSPPEKDSGL	EATRGAGGSS	SDVEGAYSRA	DEKTQDQQSL	PRPCQGQDPS	hPR
DERGD VMDFYKTLRG	SSVLAQERGD	SLTPGREENP	MDSKE	•	•	nek
•	•	•	•	•	•	ner i e i
•	•	•	•	•	•	hVDR
	•	•	•	•	•	1PPARgamma
•	•	•	•	•	•	hPPARbeta
•	•	•	•	•	•	nPPARalpha
	•	•	•	•	•	hRXRbeta
	•	•	•	•	•	hRXRalpha
	•	•	•	•	•	hRARgamma
	•	•	•	•	•	hRARalpha
	•	•	•	•	• • • • • • • • • • • • • • • • • • • •	hTRbeta
	•	•	•	•		hTRalpha
	•	•	•	•	•	rTRalpha
120					61	

FIG.3B

BY CLASS SUBCLASS

•	•	•	•	•	•	
RSFH SDSGSSVNGG		GHRPSTLSCV NTPL.	EQLYKFYKGN	SIEGGNGGGS WSFAKTIÖNA		מאל
KVGDSSGTAA	SRSGC	PPAAPATQRV		FFACEVISON	SACONOCIANS	אמ
DEFECTIVENA	A T T S		פר המתחים ביי	PSGPGOSOPS PDACEUTEST	PSGPGOSOBS	hpr
	Deropertu			PSLAVASOS.	GATVKVSASS	hGR
		•	•	•	•	hER
			•	•	•	hVDR
•			•	•	•	hPPARgamma
•			•	•	•	hPPARbeta
•			•	•	•	hPPARalpha
•			•	•	•	hRXRbeta
•			•	• • • • • • • • • • • • • • • • • • • •	•	hRXRalpha
•			•	•	•	hRARgamma
•			•	•	•	hRARalpha
•			•	•	• • • • • • • • • • • • • • • • • • • •	hTRbeta
•			•	• • • • • • • • • • • • • • • • • • • •	•	hTRalpha
100			•	•	•	rTRalpha
180					121	

BY CLASS SUBCLASS

FIG.3C

	181					3
rTRalpha	•	•	•			74
hTRalpha	•	•				•
hTRbeta	•	•	•			
hRARalpha	•	•	•	•		
hRARgamma	•	•	•	•		
hRXRalpha	•	•	•	•		
hRXRbeta	•	•	•			•
1PPARalpha	•	•	•			•
hppARbeta	•	•	•			•
1PPARgamma	•	•	•			
hVDR	•	•	•			
hER	•	•	•	•		
hGR	.QQPDLSKAVS	LSMGLYMGET	ETKVMGNDLG	FPQQGQISLS	SGETDLKLLE	LKLLE ESTANINES
hPR	AHKVLPRGLS	PARQLLLPAS	ESPHWSGAPV		SSESE	ESAGPLIKGK
hMR	VMRAIVKS	PIMCHEKSPS	VCSPLNHTSS		SFGSF	SEGSE PVHSPITOGT
har	•	•	•	•	•	

FIG.3D

DOKETIEL OBIODO

BY CLASS SUBCLASS

					hAR
PLICSPNAEN RGSRSHSPAH ASNVGSPLSS PLSSMKSSIS SPPSHCSVKS PVSSPNNVIL	PLSSMKSSIS	ASNVGSPLSS	RGSRSHSPAH	PLTCSPNAEN	hMR
ALVEQDAPMA PGRSPLATTV	EDSRFSAPRV	AAGGVALVPK	GGAAACPPGA	PRALGGAAAG	hPR
HIKGQIGING GNVKLYII	THSDVSSEQQ	AAPTEKEFPK	PKSSASTAVS	TSVPEN	hGR
•	•	•	•	•	hER
	•	•	•	•	hVDR
•	•	•	•	•	hPPARgamma
• • • • • • • • • • • • • • • • • • • •	•	•	•	•	hppARbeta
	•	•	•	•	hPPARalpha
	•	•	•	•	hRXRbeta
•	•	•	•	•	hRXRalpha
	•	•	•	•	hRARgamma
	•	•	•	•	hRARalpha
• • • • • • • • • • • • • • • • • • • •	•	•	•	•	hTRbeta
	•	•	•	•	hTRalpha
	•	•	•	•	rTRalpha
300				241	

FIG.3E

. OGGEVIER LOGIOCO

hPPARgamma hPPARalpha hPPARbeta hRXRalpha hRARgamma hRARalpha hRXRbeta hTRalpha rTRalpha hTRbeta hVDR hPR hGR **hER** RSSVSSPANI NNSRCSVSSP SNTNNRSTLS SPAASTVGSI CSPVNNAFSY TASGTSAGSS MDFIHVPILP LNHALLAART RQLLEDESYD GGAGAA.... • • • • • • • • 301DQST FDILQDLEFS • • • • • • • • SGSPGK....ET NESPWRSDLLSA FAPPRTSPCA 360

FIG.3F

,	hAR	hmr	חלא	וויי א		7 19	hVDR	hPPARgamma	hPPARbeta	hPPARalpha	hRXRbeta	hRXRalpha	hRARgamma	hRARalpha	hTRbeta	hTRalpha	rTRalpha	
			SSTPVAVGDF				•	•	•		•		•	• • • • • • • • • • • • • • • • • • • •	•	•		361
•	1	TLRDVVPSPD TQEKGAQEVP	PDCAYPPD	, AGEDDSFLLE				• • • • • • • • • • • • • • • • • • • •	•	•	•		•		•	•	•	
•			AEPKDDAYPL	GNSNEDCKPL	•			•	•	•	•	•	•	•	•	•	•	
•			YSDFQPPALK	ILPDTKPKIK	•	• • • • • • • • • • • • • • • • • • • •			•	•	WSH	•	•	•	•	•	•	
•	TAKTTAKEED		IKEEEEGAEA	DNGDLVLSSP	•	•					ď	•	•		•	•	•	
	TARBED GARBSSCLEG	Carcacto	SARSPRSYLV	SNVTLPQVKT	HIM	• • • • • • • • • • • • • • • • • • • •	•				HAEGSVGRWG							420

FIG.3G

	GA VAPYGYTRP.	GA	GGGEA	GG GGGEA	•	•	nak
	FSFMDD KDYZSLSGIL	DGSY	NPTVNPFPFM	HSCSGTSFKG	SVPIKQESTK	NOKINSUSSE	nmk
	AA PASASVSSAS		EAAVT	PR. ATPSRPG	dladadana		וויא
	NK MSAISVHGVS	NX	ANIIG	TVYCQASFPG	PGVIKQEKLG		nck
	KPAVYN YPEGAAYEFN	LDSSKPAVYN	PLERPLGEVY	EPLNRPQLKI	LLHQIQGNEL		בר ב
. •	VMSGQE TIRVLEVEVD	AQVIVMSGQE	SCTLKFPAQD		DTEDLPANNA	X	hVDR
	•	•	•	•	•	•	hPPARgamma
	•	•	•	•	•	•	hPPARbeta
	•	•	•	•	•	•	hPPARalpha
	SRSPDSSSPN	RDGRHGRD SRSPDSSSPN		AKECIVGSAT ALAGSRSGGG GGGGRRRTIN PGAGARGWIG	ALAGSRSGGG	AKECIVGSAT	hRXRbeta
	FSTQVNSS	MDTKHFLPLD FSTQVNSS	•	•	•		nkxkalpha
	•	•	•	•	•	•	hRARgamma
	•	•	•	•	•	•	hRARalpha
	•	•	•	•	•	•	hTRbeta
	•	•	•	•	•	•	hTRalpha
	•	•	•	•	•	•	rTRalpha
	480					421	

FIG.3H

hVDR hER hGR hPR hMR hAR	hPPARalpha hPPARbeta hPPARgamma	hRARalpha hRARgamma hRXRalpha hRXRbeta	rTRalpha hTRalpha hTRbeta
TALSSAGAAE AAAAANAQVY TSGGQMYHYD SSGSTLECIL GPPVPGFDGN		LISPIGR	481
SGGDEEGSGQ GQTGLPYGPG MNTASLSQQQ YKAEGAPPQQ CEGSGFPVGI PQGLAGQE		LTSPTGR GSMAAPSLHP SLGPGIGSPG	• • • • • • • • • • • • • • • • • • • •
SLEATEEAQL DGPVTTSSTT AVTVEVSAPV VQTVVSKAAI SEAAAFGSNG LGGFPPLNSV SPSPLHLLHP PPQLSPFLQF DQKPIFNVIPP IPVGSENGPFAPPPCKA PGASGCLLPR DGLPSTSKQEPDDGSYY PEASIPSSAI VGVNSGGQSF HYRIGAQGTI SDFTAPDVWY PGGMVSR VPYPSPT			
DGPVTTSSTT AVTVEVSAPV LGGFPPLNSV SPSPLHLLHP .KPIFNVIPP IPVGSEN PGASGCLLPR DGLPSTS PEASIPSSAI VGVNSGGQSF PGGMVSR VPYPSPT			540
AVTVEVSAPV VQTVVSKAAI SPSPLHLLHP PPQLSPFLQP IPVGSEN DGLPSTS VGVNSGGQSF HYRIGAQGTI VPYPSPT	QSIGEDSSGS EVAEAEGAPE LSMMDDHSHS		540MEQKPSK VECGSDPEENMEQKPSK VECGSDPEEN HCPDREHDWK LVGMSEACLH
EVSAPV VQTVVSKAAI LMLLHP PPQLSPFLQP SEN STS SGGQSF HYRIGAQGTI SPT	FGFTEYQYLG LNGGPQHALP FDIKPFTTVD	ERLFAA GALGPGSGYP NGMGPP FSVISSPMGP	540 VECGSDPEEN VECGSDPEEN LVGMSEACLH

	541					600
rTRalpha	SARSPDGKRK RKN.GQCP		LKSSM	•	•	SGYI
hTRalpha	SARSPDGKRK	RKN.GQCS	LKTSM	•	•	SGYI
hTRbeta	RKSHSERRST	LKN.EQSSPH	LIQTTWISSI	FHLDHDDVND	QSVSSAQTFQ	AQTFQ TEEKKCKGYI
hRARalpha	•	•	PN SNHVASGAGE		AAIETQSSSS	EEIVPSPPSP
hRARgamma	GAGFPFAFPG	GAGFPFAFPG ALR.GSPPFE MLSPSFRGLG QPDLPKEHAS LSVETQSTSS	MLSPSFRGLG	QPDLPKEKAS	LSVETQSTSS	EEMVPSSPSP
hRXRalpha	HSMSVP	.TTPTLGFST	GSPQLSS	.PMNPVSSSE DIKPP	DIKPPLGLNG	LGLNG VLKVPAHPSG
hRXRbeta	PGLPPP	.APPGFSGPV	.APPGFSGPV SSPQINSTVS LPGGGSGPPE		DVKPPVLGVR	VLGVR GLHCPPPPGG
nPPARalpha	SCPGSDGSVI	TDTLSPA	•	•	.SSPSSVT	YPVVPGSVDE
hppARbeta	SSSYTD	LSRS	•	•	.SSPPSLL	SLL DQLQMGC.DG
1PPARgamma	FSSISAPHYE	DIPFTRADPH VADYKYDLKL QEYQSAIKVE	VADYKYDLKL	QEYQSAIKVE	PASPPYYSEK	YYSEK AQLYNRPHEE
hVDR	SVSPAQQTSV	PITVQACPQV	LTQDGLASLM TGMLAQQSSL		GOPLLIPLSH	AGSVGGQGGL
hER	HGQQVPYYLE	NEPSGYTVRE	AGPPAF	YRPNSDNRRQ	GGRERLASTN DKGSMAMESA	DKGSMAMESA
hgr	WNRCQGSG	DDNLTSLGTL	NFPGRTVFSN	NFPGRTVFSN GYSSPSMRPD V		.SSPPSSSST
hPR	ASAAAAGA	APALYPALGL	NGLPQLGYQA	NGLPQLGYQA AVLKEGLPQV YPPYLNYLRP	YPPYLNYLRP	DSEASQSPQY
hmr	SLSRSARDQS	SLSRSARDQS FQHLSSFPPV NTLVESWKSH GDLSSRRSDG YPVLEYIPEN VSSSTLRSVS	NTLVESWKSH	GDLSSRRSDG	YPVLEYIPEN	VSSSTLRSVS
har	CVKSEMGP	CVKSEMGP WMDSYSGPYGD MRLETARDHV LPIDYYFP	PYGD	MRLETARDHV	LPIDYYFP	•

Y8 NAMSTAARO

CLASS SUBCLASS

FIG.3J

D	KOKYLCASRN D	KVFFKRAAEG	HYGALTCGSC	FUNTO LICGURASGO HYGALTOGSO KVFFKRAAEG	OTANA	אמוו
CAGRN D	QHNYLCAGRN		HYGVVTCGSC KVFFKRAVEG	TGSSKESKIC LVCGDEASGC	TGSSKPSKIC	F3.0
CAGRN D	QHNYLCAGRN		HYGVLTCGSC	LICGUEASGC	BCCCBBCKTC	FK9 7
D	KVFFKRAVEG QHNYLCAGRN D	KVFFKRAVEG				h 0 0
TN	HNDYHCPA TN	KAFFKRSIQG			NET KYC	הרט ארט ארט ארט ארט ארט ארט ארט ארט ארט א
QAVLQPQMSA	SVQTQLQAPA QAVLQPQMSA	AGLQAATVLN			AVETEPTATV	カマロス
DL	· · · RC	KGFFRRTIRL KLIYD		RVCGDKASGF	PSNSLMATEC	hPPARgamma
ER.	KLEYEKC	KGFFRRTIRM	HYGVHACEGC	RVCGDKASGF	ASCGSLNMEC	hPPARbeta
DR	KLVYDKC	KGFFRRTIRL KLVYD	HYGVHACEGC	RICGDKASGY	SPSGALNIEC	hPPARalpha
NX	KGFFKRTIRK DLTYSCRD	KGFFKRTIRK		PGAGKRLC AICGDRSSGK HYGVYSCEGC	PGAGKRLC	nRXRbeta
NK		KGFFKRTVRK	HYGVYSCEGC	NMASFTKHIC AICGDRSSGK HYGVYSCEGC KGFFKRTVRK DLTYTCRD	NMASFTKHIC	hRXRalpha
DK	KGFFRRSIQK NMVYTCHR DK	KGFFRRSIQK	HYGVSSCEGC	FVCNDKSSGY	PPPPRVYKPC	hRARgamma
VYTCHR DK	NHVYTCHR	KGFFRRSIQK NM	HYGVSACEGC	FVCQDKSSGY	PPLPRIYKPC	hRARalpha
EG	NLHPSYSCKY	KGFFRRTIQK	HYRCITCEGC	VVCGDKATGY	PSYLDKDELC	hTRbeta
DS	NLHPTYSCKY	KGFFRRTIQK	HYRCITCEGC	PSYLDKDEQC VVCGDKATGY HYRCITCEGC	PSYLDKDEQC	hTRalpha
TYSCKY DS	NLHPTYSCKY	KGFFRRTIQK NLHP	HYRCITCEGC	VVCGDKATGY	PSYLDKDEQC	rrkalpna
660					601	

rTRalpha hTRalpha hTRbeta hRARalpha hRARRalpha hRXRAlpha hPPARAlpha hPPARBeta hPPARBeta hPPARBeta hPPARBeta hPPARBAMA hPPARBAMA hAR	
CCVIDKITR NQCQLCRFKK CIAVGMAMDI CCVIDKITR NQCQLCRFKK CIAVGMAMDI KCVIDKVTR NQCQECRFKK CIYVGMATDI NCIINKVTR NRCQYCRLQK CFEVGMSKES NCIINKVTR NRCQYCRLQK CFEVGMSKES NCIINKVTR NRCQYCRYQK CLAHGMKREA CCTVDKRQR NRCQYCRFHK CLSVGMSHNA SCKIQKKNR NKCQYCRFQK CLALGMSHNA NCRIHKKSR NKCQYCRFQK CLALGMSHNA NCRIHKKSR NKCQYCRFQK CLAVGMSHNA CQAMQQTQTT AATTASIVQK ASEPSVSVAT QCTIDKNRR KSCQACRLRK CYEVGMMKGG CIIDKIRR KNCPACRYRK CLQAGMNLEA CCIIDKIRR KNCPACRLQK CLQAGMNLGA CCIIDKIRR KNCPACRLQK CLQAGMNLGA CCIIDKIRR KNCPACRLQK CLQAGMNLGA	661
VLDDSKRVAK RKL VLDDSKRVAK RKL VLDDSKRLAK RKL VRND	
LIEQNRER RRK. EEMIR LIEQNRER RRK. EEMIR LIEENREK RRR. EELQKRNK KKK. EVPKPRNK KKK. EVFKPRNK KKK. EVFKPRNK LVA. EILTC LPEAEKRK LVA. EILSS SAASLGA QPQFISSLTT KRQRDDG EGR. GEVGS KK. KIK GIQ. QATT. KKFNKVR VVR. ALDAV KKLGKLK GIH. EEQPQ	3

FIG.3L

hPPARgamma hPPARalpha hPPARbeta hRXRalpha hRARgamma hRARalpha hRXRbeta hTRalpha rTRalpha hTRbeta **hVDR** RMA RMA hPR hER hGR STT\$P..... TEETTQKLT VSHIEGYECQ PIFLN.... VL...... QQQ\$PPPPPP PQSPEEGTTY IAPAKEPSVN TALVPQLSTI SRALTPSPVM VL...... GVSQ ETSENPGNKT IVPATLPQLT AGDHRAANLW PSPLMIKRSK KNSLALSLTA DQMVSALLDA EPPILYSE...... TPI ITSAMSN VAGLTSQLIT NAQGQVIGTL PLLVNPASLA GAAAASA...LPA DIDQLNPESA DLRALAKHLY DSYIKSFP.L TKAKARAILT GKTTDKSPFV IYDHNSLMHG EGSQYNPQVA DLKAFSKHIY NAYLKNFN.M TKKKARSILT GKASHTAPFV IHDIETLWQA PEEMPVDRIL EAELAVEQKS DQGVEGPGGT GGSGS.... GSP¶SYELSP QLEELITKVS KAHQETFPSL CQL...GKYT TNSSADHRV. ECS#SYTLTP EVGELIEKVR KAHQETFPAL CQL...GKYT TNNSSEQRV. EHD¶EDSETA DLKSLAKRIY EAYLKNFN.H NKVKARVILS GKASNNPPFV IHDHETLCHA NEDHPVERIL EAELAVEPKT ETYVE..ANH GLNPS.....SP.. SIGHKPEPTD SLOGRPEPTP EEWDLIHIAT EAHRSTNAQG SHWKQRRKFL PDDIGQSPIV SLOGRPEPTP EEWDLIHVAT EAHRSTNAQG SHWKQRRKFL PDDIGQSPIV EEWELIKTVT EAHVATNAQG SHWKQKPKFL PEDIGQAPIV PTLVS..... LL.....SP.. • • • • • • • • • •

r minimal start site 725

FIG.3M

FIG.3N

LPCEDQIILL LPCEDQIILL LSIADQITLL LPLDDQVILL LPLDDQVILL LPLNDQVILL LPLNDQVTLL LTLHDQVTLL LHLDDQMTLL LHLDDQMTLL LHLDDQMTLL LHLDDQMTLL LHLDDQMTLL	ITPAITRVVD FAKKLPHFSE LPCEDQIILL ITPAITRVVD FAKKLPHFCE LPCEDQIILL STKCIIKIVE FAKQLPGFTT LTIADQITLL ATKCIIKIVE FAKRLPGFTG LSIADQITLL ADKQLFTLVE WAKRIPHFSE LPLDDQVILL SVETVTELTE FAKAIPAFAN LDLNDQVTLL TVETVRELTE FAKAIPAFAN LDLNDQVTLL SVEAVQEITE YAKNIPGFIN LDLNDQVTLL SVEAVQEITE YAKNIPGFIN LTLHDQVTLL AIPSTASVLP KATVPLTLTK TTTQGPVGKV ADRELVHMIN WAKRVPGFVD LTLHDQVHLL GGRQVIAAVK WAKAIPGFRN LHLDDQMTLL GGRQLLSVVK WAKSLPGFRN LHLDDQMTLL AGKQHIQVVK WAKVLPGFKN LPLEDQITLI AGKQHIQVVK WAKALPGFRN LHVDDQMAVI	ITPAITRVVD FAKKLPMFSE ITPAITRVVD FAKKLPMFCE STKCIIKIVE FAKQLPGFTT ATKCIIKIVE FAKRLPGFTG ADKQLFTLVE WAKRIPHFSE ADKQLFTLVE WAKRIPHFSS SVETVTELTE FAKAIPAFAN TVETVRELTE FAKAIPAFAN TVETVRELTE YAKNIPGFIN AIPSTASVLP KATVPLTLTK ADRELVHMIN WAKRVPGFVD GGRQVIAAVK WAKAIPGFRN GERQLLSVVK WAKVLPGFRN AGKQMIQVVK WAKALPGFRN	. SMPDGDKVD LEAFSEFTKI ITPAITRVVD .NAPEGGKVD LEAFSHFTKI ITPAITRVVDSLD IDLWDKFSEL STKCIIKTVEQLD LGLWDKFSEL ATKCIIKIVE .NDPVTNICQ AADKQLFTLVE .NDPVTNICQ AADKQLFTLVE .NDPVTNICQ AADKQLFTLVE .NGLPYKEIS VHVFYRCQCT SVETVTELTE PLQEQSKEVA IRIFQGCQFR SVEAVQEITE QLLLNSQGQI IATIGNGPTA AIPSTASVLP .YDPTRPFSE ASMMGLLTNL ADRELVHMIN GYDSSVPDST WRIMTTLNML GGRQVIAAVK GHDNTKPDTS SSLLTSLNQL GERQLLSVVK GYDSSKPDTA ENLLSTLNRL AGKQMIQVVK	 EKTLVAKLVA EKGLVWKQLV EDKIKFKHIT QGLQVQTVAP EVIEPEVLYA ENIEPEIVYA ENIEPEIVYA EAIEPGVVCA	hTRbeta hRARalpha hRARgamma hRXRalpha hRXRbeta hPPARgamma hPPARgamma hPPARgamma hPPARgamma hPPARgamma hWDR hER hGR hPR
LPCEDQIII	FAKKLPHFSE LPCEDQIILL	ITPAITRVVD	.SMPDGDKVD LEAFSEFTKI	•	rTRalpha
840				101	•

hAR	her.	hPR	ngr	nek	hVDR	nPPAKgamma	nrrakbeta	nPPAKaipha	nkkkbeta	nexkalpha	nkakgamma	nkakalpha	nïkbeta	nTRalpha	rrkalpna	
QYSWMGLMVF	QYSWMCLSSF	QYSWHSLKVF	QYSWHFLMAF	ECAWLEILMI	APSKVIIAPQ	KYGVHEIIYT	KYGVHEAIFA	KYGVYEAIFA	RAGWNELLIA	RAGWNELLIA				KGCCMEIMSL	KGCCMEIMSL	841
QYSWMGLMVF AMGWRSFINV NSRMLYFAPD LVFNEYRMH.	ALSWRSYKHT NSOFLYFAPD	GLGWRSYKHV	ALGWRSYRQS	GLVWRSME	APSKVIIAPQ PSVVKPVTSL	KYGVHEIIYT MLASLMNK DGVLISEGQG	KYGVHEAIFA MLASIVNK DGLLVANGSG F.VTREFLR.	KYGVYEAIFA MISSVMNK DGMIVAYGNG	SFSHRSID VRDGILLATG			RICTRYTP EQDIMITSDG				
NSRMLYFAPD		SGQMLYFAPD	SANLLCFAPD	HPGKLLFAPN	TAAGVIACGE	DGVLISEGQG	DGLLVANGSG	DGMLVAYGNG	VRDGILLATG	VKDGILLATG	EQUIMIFSDG	EQDIMITSDG	RAAVRYDP ESETLTLNGE		RAAVRYDP ESDTLTLSGE MTVKRKQLK.	
LVFNEYRMH.	LVFNEEKMH.	LILNEQRMK.	LIINEQRHT.	LLLDRNQGK.	MPTVGQLVNK	F.MTREFLK.	F.VTREFLR.	F. ITREFLK.	LHVHRNSAH.	LHVHRNSAH.	LTLNRTQMH.	LTLNRTQMH.	MAVIRGQLK.	MAVKREQLK.	HTVKRKQLK.	
KSRMYS QCVRMRHLSQ	OSAMYE I COCMHOTST	ESSFYS	LPCMYD QCKHMLYVSS	CVEGMVEI FDMLLAT.SS	PSAVKDEEAI NLEEIREFAK	SLRKPFGD	SLRKPFSD	SLRKPFCD	S.AGVGAI	S.AGVGAI	NAGFGP	NAGFGP	NGGLGV	NGGLGV	NGGLGV	
QCVRMRHLSQ	T.COCMHOTST	LCLIMWOIPO	QCKHMLYVSS	FDMLLAT.SS	NLEEIREFAK	FMEPKFEFAU	IIEPKFEFAV	IMEPKFDFAM	FDRVLTELVS	AGVGAI FDRVLTELVS	AGEGP LIDLVFAFAG	LTDLVFAFAN	GGLGV VSDAIFDLGH	.GGLGV VSDAIFELGK	.GGLGV VSDAIFELGK	900

DAMSTHARD

Y8

CLASS SUBCLASS

rTRalpha hTRalpha hTRalpha hTRbeta hRARalpha hRARGamma hRXRalpha hPPARAlpha hPPARGamma hPPARGamma hPPARGamma hPPARGamma hPPARBeta hPPARGamma hPR
SUSAFNIDDT SISAFNIDDT SISAFNIDDT SISSFNIDDT QLIPIEMDDA QLIPIEMDDT KMRDMRMDKT KMRDMRMDKT KFNALELDDS KFNALELDDS KFNALELDDS KFNALELDDS EFFWHNIQGE EFFWKLQVSYE EFFVKLQVSYE EFFVKLQVSYE EFFWRLQITFE
EVALLQAVIL EVALLQAVIL EVALLQAVIL ETGILSAICL ETGILSAICL ETGLLSAICL ELGCLRAIVI ELGCLRAIII DIALFIAAII DLAIFIAVII LTQTQVGQAL EFVCKXTLLL EYLCKXVLLL EYLCKXVLLL EYTIKVVLLL EYTIKVLLL
SQEAYL LAFEHYV KSQEAYL LAFEHYV KSQEAYL LAFEHYV KYQDSFL LAFEHYI MLQEPLL EALRLYA ALREKVY ASLEAYC VLREKVY ASLETYC KMQEGIV HVLRLHL AIQDTIL RALEFHL DIQDNLL QALELQL KSAQKLK PVLERWLAEA RVLDKIT DTLIHLMAKA SIRMTYI KELGKAIVKR EMRSSYI RELIKAIGLR EMRTNYI KELRKMVTKC LRMNYI KELDRIIACK

DFPEMMAEII	IKSHMVSV DFPEMMAEII	ELHQFTFDLL	LLDSVQPIAR	FYQLTK	KKNPTSCSRR FYQLTK LLDSVQPIAR ELHQFTFDLL	IIAR
EFPAMLVEII	RESHALKV EFPAMLVEII	DLLEFCFYTF	LLDSMHDLVS	FYQLTK LLDSMHDLVS	PNNUGOSWOR	ביין ביין
EFPEKMSEVI	IQSRALSV EFPEMMSEVI		LLDNLHDLVK	FYOLTK LLDNLHDLVK QLHLYCLNTF		האל
EFPEMLAEII	LD.KTMSI		LLDSMHEVVE	FYQLTK		ה מל א
PLYDLLLEML	MKC.KNVV			LAQLLL	GLTLQQQHQR FCWGGQHQR	ה ה ה
EITEIAKELN	FEKNSLPTGQ	PQAIEVLNTY	KKRKRRTSFT PQAIEVLNTY			カマロス
SLHPLLQEIY	EHVQLLHV IKKTETDM	EHVQLLHV	KMTDLRQIVT			hPPARgamma
SLHPLLQEIY	EHAQMMQR IKKTETET SLHPLLQEIY	EHAQMMQR	KMADLRQLVT	FPKLLQ KMADLRQLVT		nPPARbeta
ALHPLLQEIY	IKKTESDA	EHAQLVQI	KMADLRQLVT	FPKLLQ		nPPARaipha
PIDTFLMEML	FKL.IGDT	KCLEHLFF	RLPALRSIGL	KOKYPEQQGR FAKLLL	KOKYPEQQGR	nkakbeta
PIDTFLMEML	KCLEHLFF FKL.IGDT	KCLEHLFF	RLPALRSIGL	FAKLLL RLPALRSIGL	KHKYPEQPGR	haxalpha
M. PPLIREML	KGAERAIT LKMEIPGP M.PPLIREML	KGAERAIT		FPRMLM KITDLRGIST		hrangamma
H. PPLIQEML	KGAERVIT LKMEIPGS M.PPLIQEML	KGAERVIT		FPKML	RKKKPSKPHM	hRAKaipna
LLPPLFLEVF	MKVECPIE	CHASRFLH	KVTDLRHIGA	NIKKHHVIHF WPKILM	NIRKHHVIHF	hanaleta
LFPPLFLEVF	MKVECPTE	CHASRFLH	KVTDLRMIGA	NHKKHNIPHF WPKLL KVTDLRMIGA	NHKKHNIPHE	nikaipna
LFPPLFLEVF	CHASRFLH MKVECPTE LFPPLFLEVF	CHASRFLH		NHKKHNIPHF WPKLL KVTDLRMIGA	NHRKHNIPHF	rikaipna
1020					961	

FIG.3Q

hPPARgamma hPPARalpha hPPARbeta hRARgamma hRXRalpha hRARalpha hRXRbeta hTRalpha rTRalpha hTRbeta hVDR EMA EMA hGR SVQVFKILSG KVKPIYFHTQ SDQLPKVESG NAKPLYFHRK AAQLEKILAG MVKPLLEHKK TNQIPKYSNG NIKKLLFHQK DAHRIHAPTS YDREVVRVWF CNRRQTLKNT SKINVFQSQ. KDLY.|.... KDMY..... RDMY.... EAPHQLA... EAPHOMT... ENPEMFEDDS SQPGPHPNAS SEDEVPGGQG KGGLKSPA....... ENSEGLDTLS GOPGGGGRDG GGLAPPPGSC SPSLSPSSNR SSPATHSP.. ED...|.... EDQEVI.... EDQEV 1021 厂 minimal end site 1025 RGGASVEETD QSHLATAGST SSHSLQKYYI TGEAEGFPAT V ••••••••••••••••••••••••••••••• •••••••• ••••••• • • • • • • • • •••••••

FIG.3R

socr: <5>

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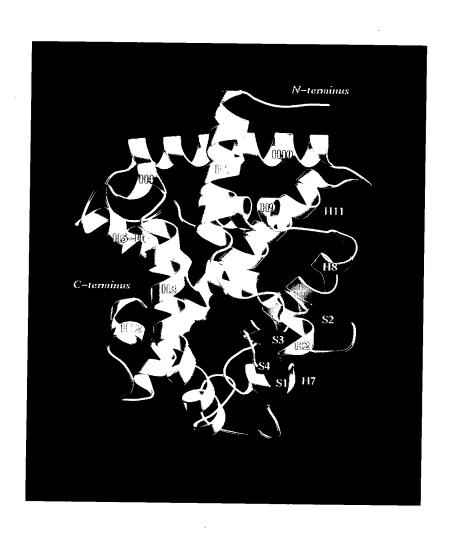
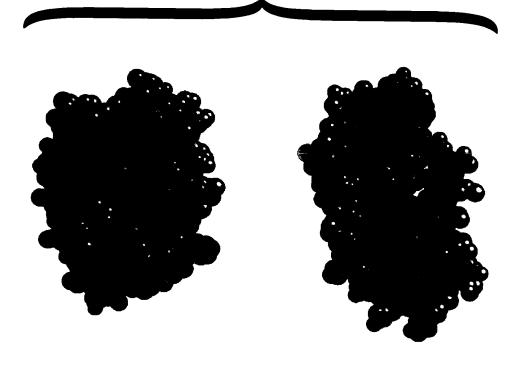


FIG. 4







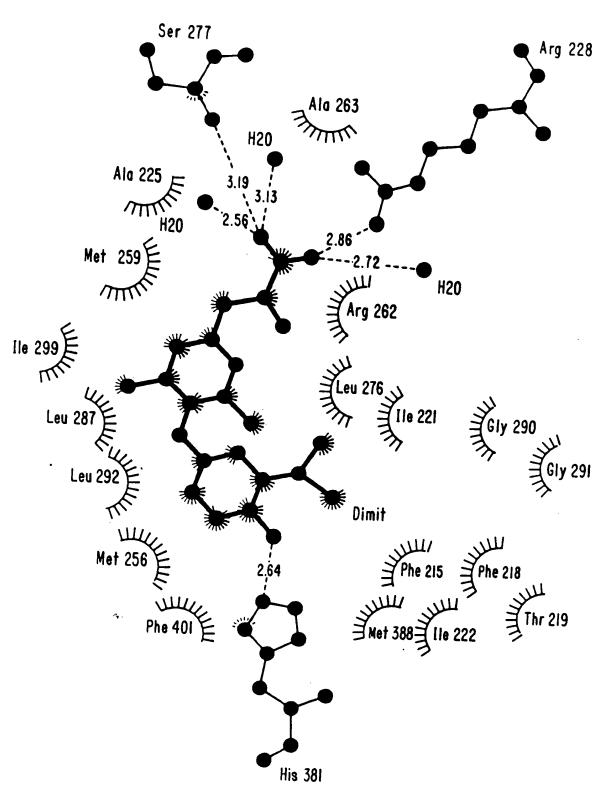


FIG.6

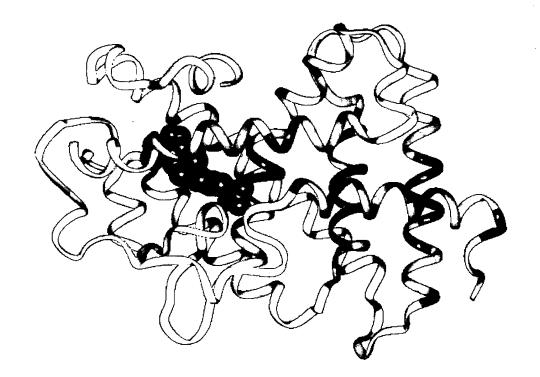


FIG. 7



FIG.8

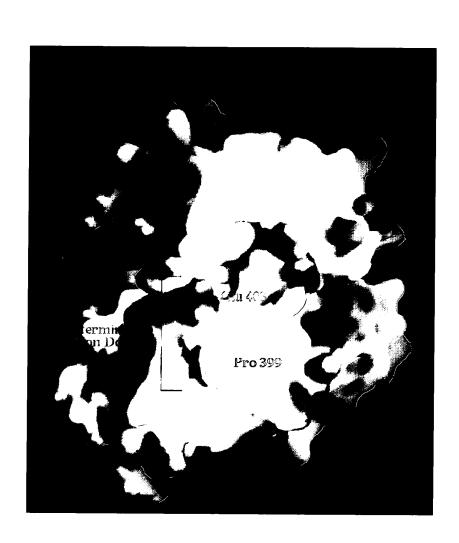


FIG. 9

AGONISTS

Retinoic Acid

Diethylstilbestrol

Progesterone

<u>ANTAGONISTS</u>

TamoxIfen

compouna	RCOX
TSI	Ph2CHCO2NHS
TS2	C ₁₆ H ₃₃ CO ₂ NHS
TS3	FMOC-CI
TS4	tB0C ₂ 0
TS5	tB0C20

ngsziszinainn

DOSIZIBE DBIDO

NO₂

TS-7

FIG.12

`C0₂H

APPROVED	O.G. F	IG.
BY	CLASS	SUBCLASS
DRAFTSMAN		•

Ph2CHNH2 TBTU, Et3N

FIG.13

15-5

I. nCg H 17 MgX

2.H₂,Pd

FIG. 14A

FIG.14B

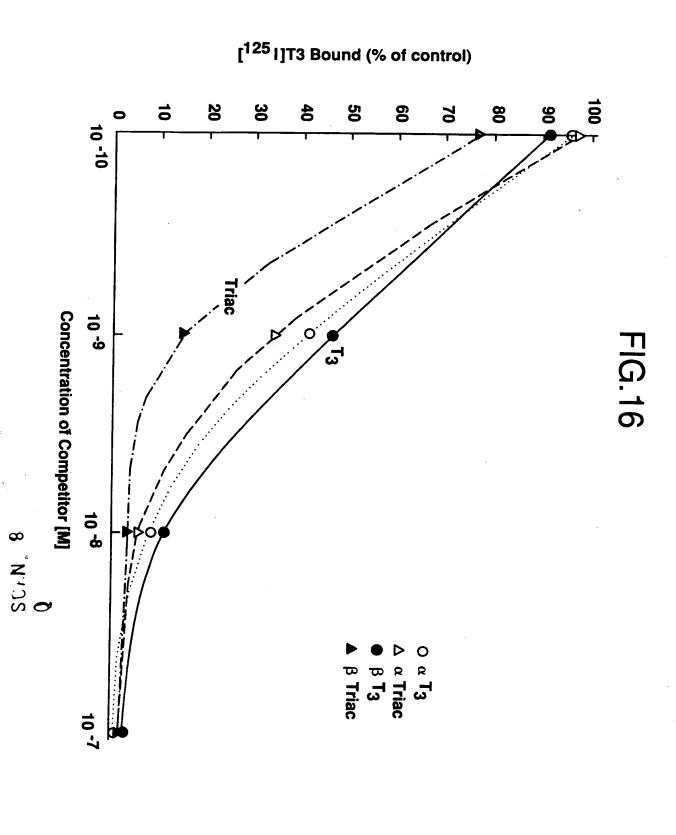
$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

$$\begin{array}{c|c} O_2N & & & \\ & N & \\ & & \\$$

TS-6

HO
$$\longrightarrow$$
 0 \longrightarrow NH 0 \longrightarrow TS-8 Ph Ph

FIG.15



BY CLASS SUBCLASS

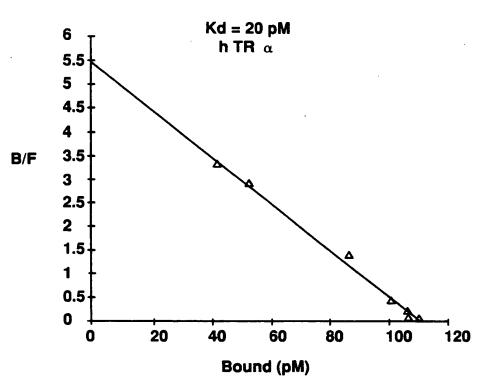
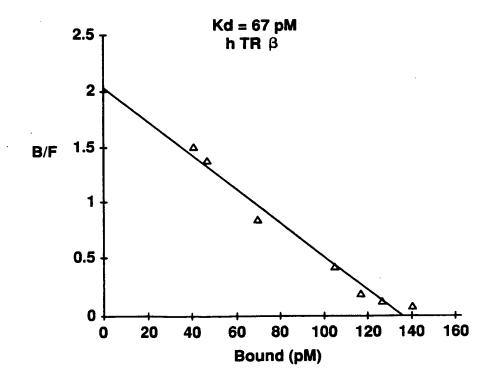
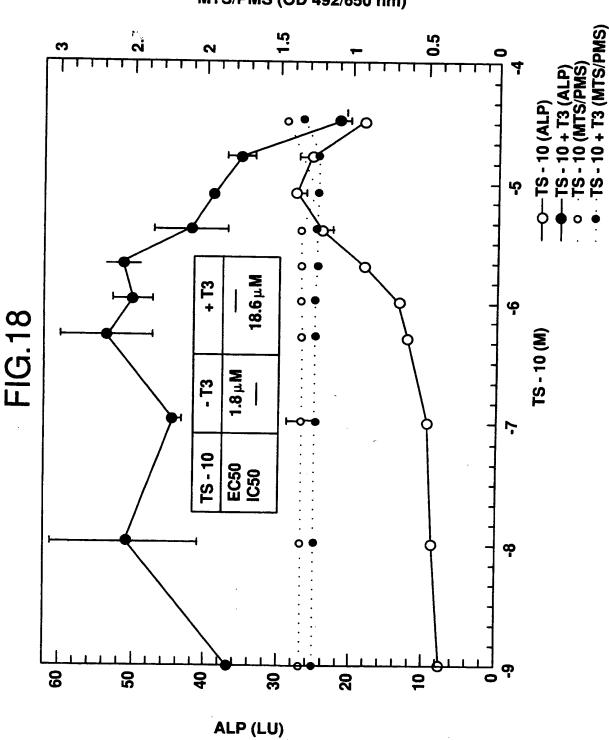


FIG.17B

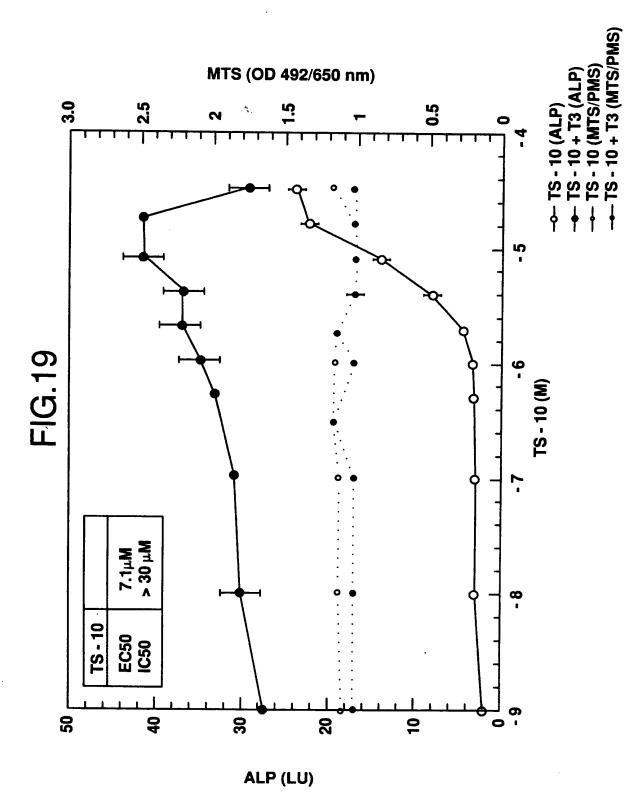


Desylandand

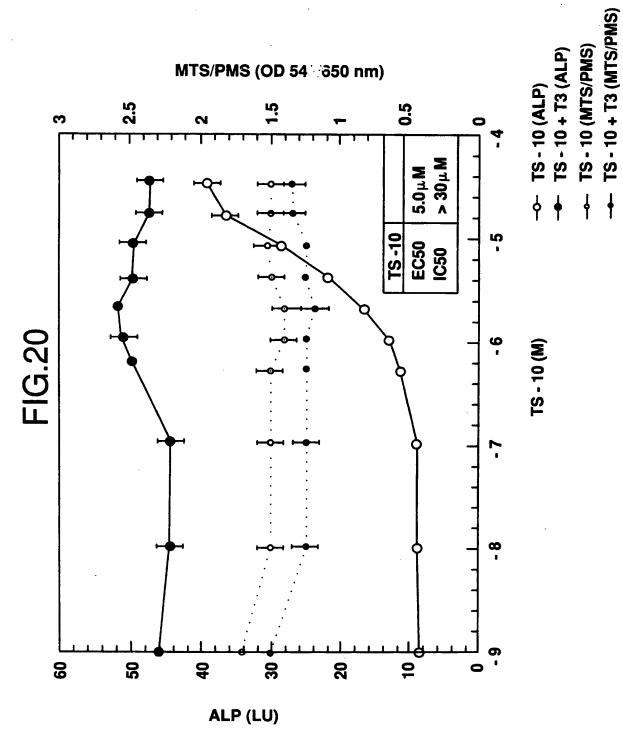




ngesylse oganon



DOEBYARE DEIDO





"(F78)1.

FIG. 21

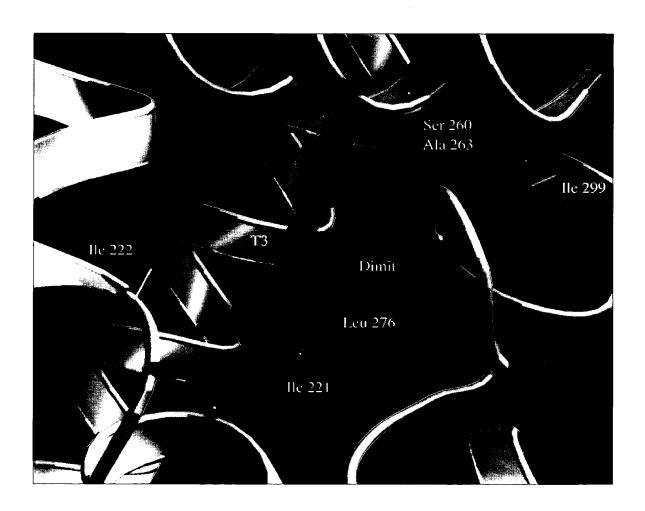


FIG. 22

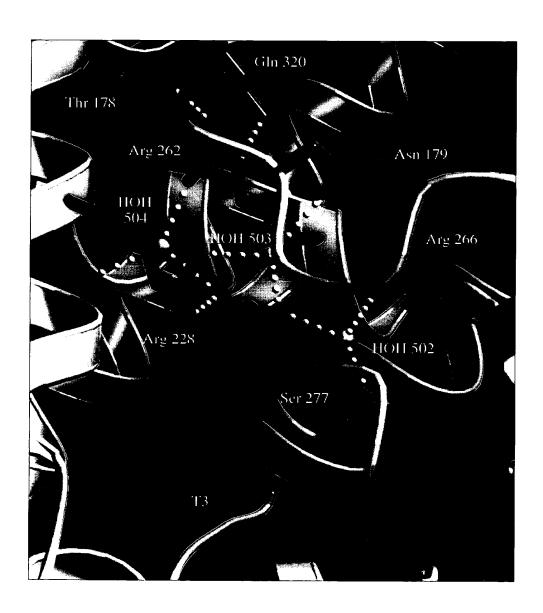


FIG. 23

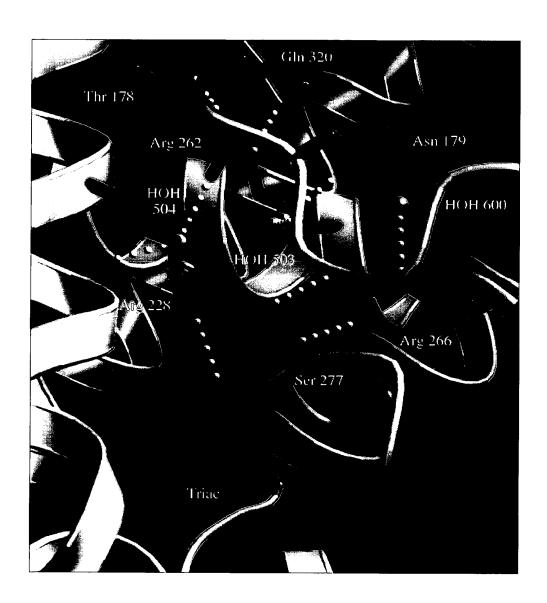


FIG. 24

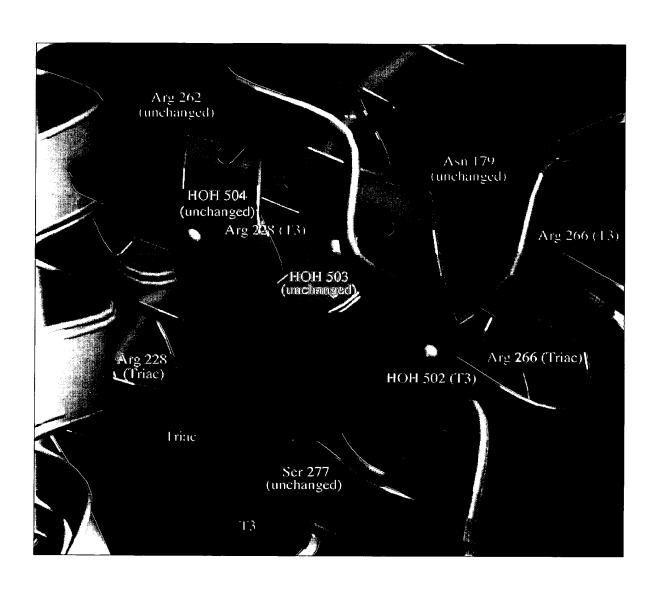


FIG. 25

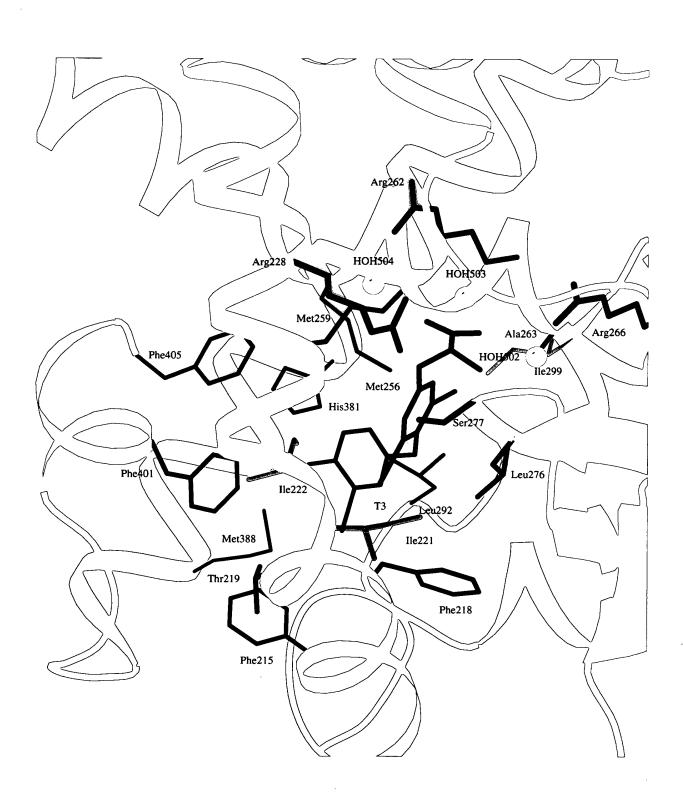


FIG. 26A

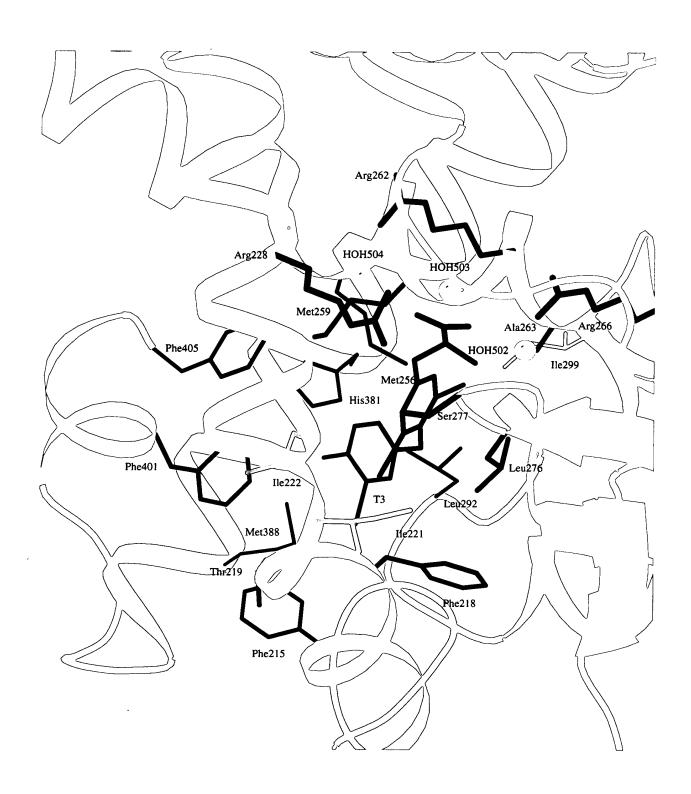
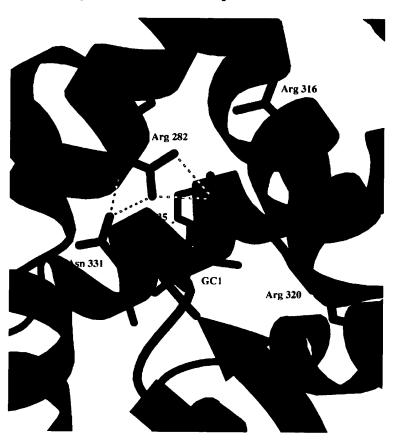


FIG. 26B

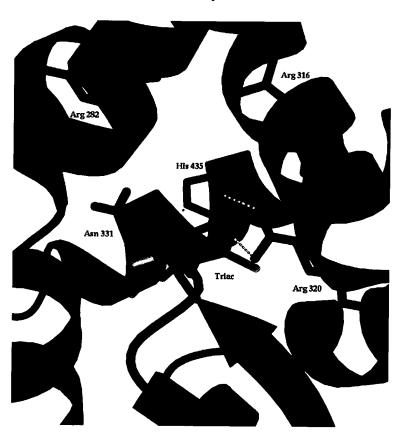
Thyroid Hormone Receptor Beta with GC1

JVĒL



-TSMAN

Thyroid Hormone Receptor Beta with Triac



Structural Differences Between TR-b with GC1 and TR-a with Dimit



Structural Differences between TR LBD isoforms with Triac

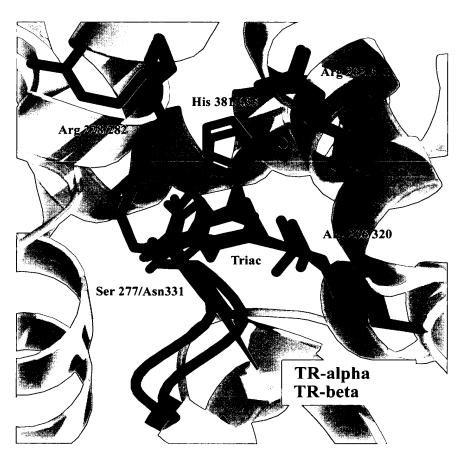
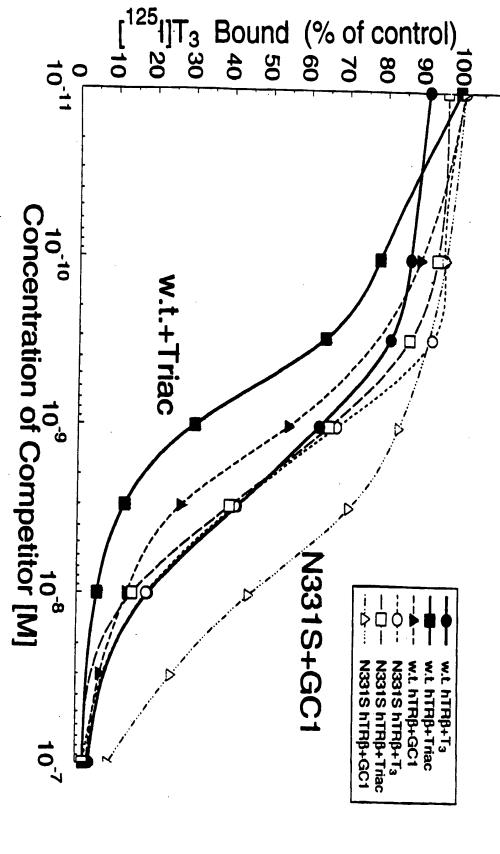


FIG.31

Competition by T₃, Triac & GC1 for [125 I]T $_3$ binding to wild type and N331S hTR β



PPPFTSMANI O G. FIG.

BY CLASS SUBCLASS MARTSMANI

DRAFTSMAN





Atomic Numbering for Thyronine-like Ligands

Ligand	R1	R3	R5	X	R3'	R4'
Dimit	amino propionic	C19	C20	O2	iPr	O1
IpBr ₂	amino propionic	BR1	BR2	O 2	iPr	O 1
Ť,	amino propionic	I1	I3	02	12	O 1
Triac	acetic acid	I1	13	O2	I2	O 1
GC1	oxyacetic acid	C19	C20	C21	iPr	O 1

amino propionic acid

acetic acid

oxyacetic acid

isopropyl

FIG.32

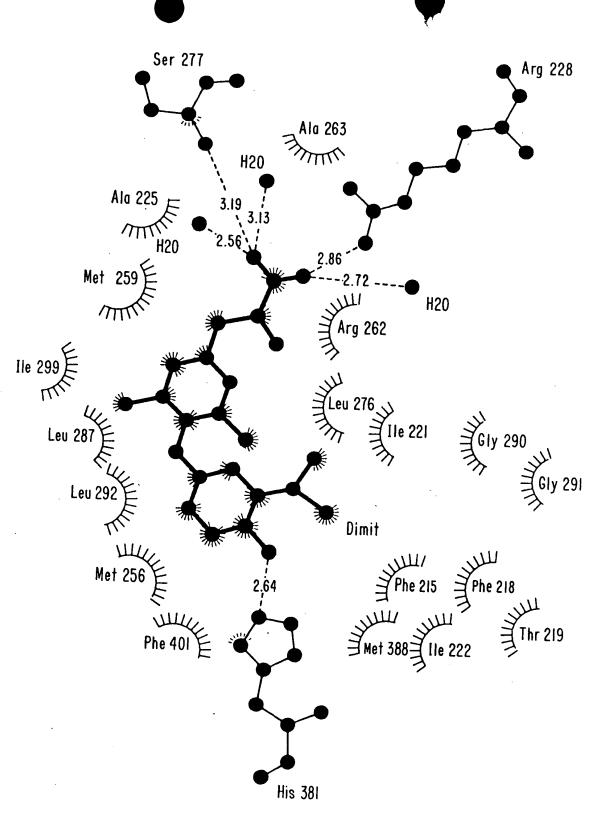


FIG.6

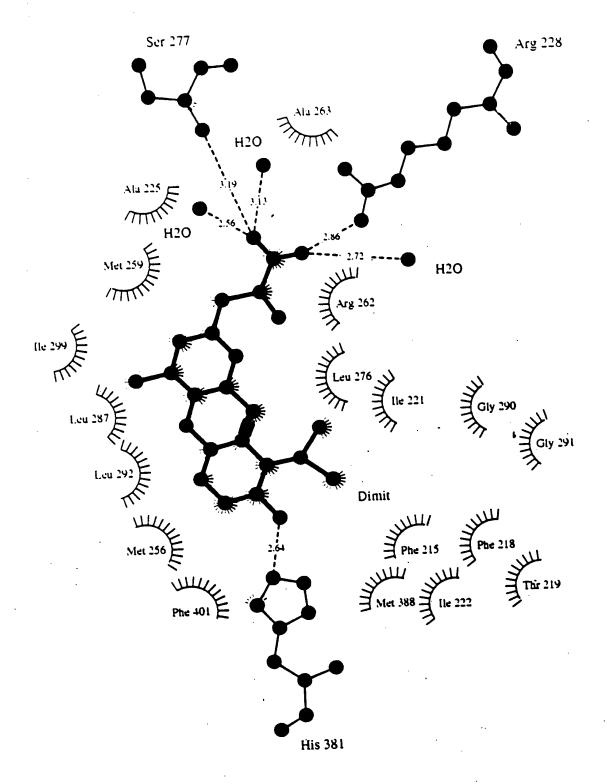


Figure 6